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SILVER SALTS AND OTHER ANTISEPTICS ON
THE DYSENTERY BACILLUS



BY

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IN Calcutta at the present time chronic bacillary dysentery is the most difficult common tropical disease to treat successfully and has the highest case mortality, with the single exception of the terrible kala-azar. The unfortunate patients usually come to hospital with extensive ulceration of the large bowel, not having been under skilled treatment during the early, and usually readily curable, stages of the disease. An analysis of the records of considerably over one hundred *post mortems* made by me on dysentery cases at the Calcutta Medical College Hospital during the last thirteen years has revealed some interesting facts, and led to an investigation with a view to finding better methods of treatment of the above-mentioned class of cases. As the *post mortem* data have been fully dealt with in a small work on dysenteries now in the press, it will only be necessary here to mention the chief points bearing on the present enquiry. I need only state in passing that no one who has had the advantage of making numerous autopsies in places in which amoebic dysentery is as common as in Calcutta, can fail to recognize at a glance the characteristic lesions of the amoebic and bacillary forms respectively, while in a great many of the cases here dealt with microscopical and bacteriological examinations were also made. Some coloured drawings illustrating the different forms will appear in my book.

THE DISTRIBUTION OF THE LESIONS IN THE LARGE BOWEL
IN ACUTE AND CHRONIC BACILLARY DYSENTERY
RESPECTIVELY.

THE most important point is the variation in the distribution of the lesions in acute and chronic cases respectively. This is well brought out in a diagram which will appear in my book, in which the portions of the mucous membrane affected in a series of cases is shown by shading. The division into acute and chronic cases is necessarily an artificial one, but the former include those in which the symptoms had lasted less than one month, and the latter those of from one month to over a year in duration. The striking feature of the acute series was that the whole, or nearly the whole, length of the large bowel was involved, while in the great majority of the cases in which the lesions reached the cæcum the lowest part of the ileum was also affected. Microscopically the process is found to be essentially an acute diphtheritic fibrinous inflammation of the mucous coat, with or without some superficial ulceration, the microscopical characters of which are described and illustrated in the work already mentioned.

On the other hand, the chronic series revealed a very different state of affairs. In the majority of them the lesions were limited to the lower half of the great bowel, while in the small number in which the disease extended above the descending colon the lesions were much less extensive in the upper part, so that the brunt of the disease was almost invariably borne by the descending colon, sigmoid and rectum. In the affected portions the mucous membrane was uniformly thickened and studded with very numerous small circular or serpiginous depressed ulcers, sometimes with but little remaining mucous membrane between them. It will be observed that these changes are in marked contrast with those of amœbic dysentery, which are also described and illustrated in my book. It would appear, from the above facts, that if an acute bacillary dysentery seriously involves the whole of the mucous membrane of the large intestine it is likely to prove rapidly fatal; but if only the lower and less vital part of the bowel is attacked, the disease commonly runs on into a chronic ulcerative condition, especially in patients who have not received adequate early treatment.

The bearing of the above facts on the local treatment of bacillary dysentery will be evident. Apart from serums and medicines administered by the mouth, we require agents which, when injected into the

bowel, will destroy the dysentery bacillus and its toxins and heal the ulcers. In the chronic cases, with ulceration limited to the lower half of the large intestine, but little can be expected from drugs given by the mouth, for, by the time they reach the ulcerated surfaces, they will quickly be expelled by the irritable bowel. On the other hand, it is just in these cases of lower gut involvement that medicated enemata may be expected to be of the greatest service. The well-established reputation of injections of silver nitrate in certain forms of chronic dysentery appears to be based on their success in some such cases. Silver nitrate, however, has the disadvantages of being precipitated by chlorides and organic matter, which render it most uncertain in its action, while its injection in sufficient strength is often very painful.

The foregoing considerations have led me to investigate the bactericidal action of organic silver salts and other antiseptics on the Shiga bacillus, in the hope of finding indications for the more efficient local treatment of intractable chronic bacillary dysentery.

METHODS OF INVESTIGATION.

Two classes of substances have been tested. Firstly, the astringent silver and copper salts and their organic compounds, which may be expected to have a healing effect on the ulcers in addition to a destructive one on the causative bacteria. Secondly, antiseptics used for their bactericidal action. Among the latter have been included the permanganates, which I have shown to have a destructive action on the toxins of the Shiga bacillus, and to be useful in acute bacillary dysentery, although their antiseptic action is very weak in the presence of organic matter.

As the bactericidal action of many substances is one thing in simple solution in a test tube, and quite another in the presence of organic matter and salts in the bowel, two sets of solutions have been used in each trial. Each set contained the same strengths of the substance being tested, but whereas in the first the solvent was sterile distilled water, in the second set half of the diluting fluid in each tube consisted of sterile broth containing chlorides and organic nitrogenous matter. Each tube contained 2 c.c. of the dilution, which varied from 1 in 100 to 1 in 5,000, and in some cases higher dilutions as shown in the tables. One-day broth cultures of Shiga's bacillus were used, and a platinum loop-ful exposed to the action of the chemicals for five minutes, and then a loop-ful of the fluid inoculated into broth in the usual way and incubated at

37° C. for two days. Any tubes in which growth appeared were sub-cultured to ascertain if the dysentery bacillus were present or not. The results are given in the accompanying tables for each class of antiseptic, arranged according to the strength of their action in the presence of salts and organic matter.

TABLE I.

Bactericidal effect of silver, copper, and mercury compounds on the dysentery bacillus.

		Dissolved in water.							Dissolved in broth.						
		1-100	1-250	1-500	1-1000	1-2500	1-5000	1-7500	1-10,000	1-100	1-250	1-500	1-1,000	1-2,500	
Albargin	...	-	-	-	-	-	-	-	-	-	-	-	+	+	No precipitate.
Do	...	-	-	-	-	-	-	-	+	-	-	-	+	+	do.
Nargol	...	-	-	-	-	-	+	-	-	-	-	+	+	+	do.
Do	...	-	-	-	-	-	-	-	-	-	-	+	+	-	do.
Protargol	...	-	-	-	-	-	-	-	-	-	-	+	+	+	do.
Do	...	-	-	-	-	-	-	-	-	-	+	+	+	-	do.
Mercuriol	...	-	-	-	-	-	-	-	-	-	-	+	+	+	do.
Silver nitrate	...	-	-	-	-	-	-	-	-	+	+	-	+	+	Precipitated.
Do	...	-	-	-	-	-	-	-	-	-	-	+	-	-	do.
Copper sulphate	...	-	-	-	-	-	-	-	-	-	-	+	+	+	do.
Argentamin	...	-	-	-	-	-	+	-	-	-	-	+	+	+	do.
Collargol	...	-	-	-	-	-	+	-	-	+	+	+	+	+	do.
Ichthargan	...	-	-	-	-	-	+	-	-	+	+	+	+	+	do.
Argyrol	...	-	-	+	+	-	+	-	-	+	+	+	+	+	No precipitate.
Cuprol	...	+	+	+	+	+	+	-	-	+	+	+	+	+	do.

TABLE II.

Bactericidal effect of some antiseptics on the dysentery bacillus.

	Dissolved in water.						Dissolved in broth.						
	1-100	1-250	1-500	1-1,000	1-2,500	1-5,000	1-100	1-250	1-500	1-1,000	1-2,500	1-5,000	
Cyllin	-	-	-	-	+	+	-	-	-	-	-	+	No precipitate.
Iodine in potassium iodide	-	-	-	-	-	-	-	-	-	-	+	+	Slight precipitate.
Izal	-	-	-	-	+	+	-	-	-	-	+	+	
Lysol	-	-	-	+	+	+	-	+	+	+	+	+	No precipitate.
Potassium permanganate	-	-	-	-	-	+	+	+	+	+	+	+	Precipitated.
Calcium permanganate ...	-	-	-	-	-	+	+	+	+	+	+	+	Precipitated.
Boracic acid	+	+	+	+	+	+	+	+	+	+	+	+	
Quinine-bisulphate ...	+	-	+	+	+	+	-	+	+	+	+	+	

THE RESULTS OF THE INVESTIGATION.

THE results obtained are so clearly shown in the tables that they require but little comment.

Silver nitrate.—The most striking point is the remarkable difference in the bactericidal power of silver nitrate against the dysentery bacillus when dissolved in water and dilute broth respectively. In the former it killed the organism in five minutes in dilutions up to 1 in 10,000, the weakest solution tested. On the other hand, with the addition of a little organic matter and salts in the added broth, in one experiment it failed in a strength of 1 in 100 and in another in one of 1 in 500, showing great weakening and irregularity in its effects. The frequent failure of silver nitrate injections in dysentery is thus easily understood.

Organic silver compounds.—With the exception of argyrol, all those tested had a considerable bactericidal action against the dysentery bacillus when dissolved in water, being effective in five minutes in dilutions of 1 in 2,500 and upwards. In the presence of a little broth, however, their action was always weaker, but in a variable degree. In the last column of the tables is entered whether any precipitate occurred in the tubes to which broth was added, and it will be found that as a general

rule those substances which produced such a precipitate acted most feebly in the presence of organic matter and salts, while those in which no such change was produced acted best.

Albargin, or silver gelatose, and nargol, or silver nucleate, gave the best results in the presence of broth, as they killed the dysentery bacillus within five minutes in a dilution of 1 in 500, or about one grain to an ounce, while protargol gave a similar result in one experiment, although it was less efficient in a second trial. Mercurool, or mercury nucleate, yielded a similar result, but it would not appear to me advisable to inject a mercury compound into the bowel in the subjects of chronic dysentery.

Argentamin (silver phosphate dissolved in ethylenediamine solution) was only active in a 1 in 250 solution in weak broth and is not so active or so convenient a preparation as the foregoing.

The remaining three silver preparations, collargol, ichthargan, and argyrol, had little or no action in the presence of broth on the dysentery bacillus.

Copper sulphate has been recommended as a bowel wash in dysentery, but although quite active when dissolved in distilled water, it only proved effective in the presence of organic matter and salts of broth in a dilution of 1 in 250, while its organic compound cuprol, or copper nucleate, prove to have no bactericidal action even in distilled water.

Table II shows the action of certain antiseptics on the dysentery bacillus. The most active was cyllin, which was at least equally effective in broth as in distilled water. The broth tube inoculated from the 1 in 2,500 dilution in distilled water only showed growth on the second day, so but very few organisms could have survived. A solution of iodine in iodide of potassium, in the proportion of one of the former to two of the latter, and also izal gave practically as good results as cyllin, all three being effective up to dilutions of 1 in 1,000. Lysol, on the other hand, gave a disappointing result in the one test made.

Both potassium and calcium permanganate were effective up to a 1 in 2,500 solution in water, but completely failed in the presence of broth, being precipitated and rendered inert by the organic matter present.

Boracic acid and quinine-bisulphate (which has been so much used as a bowel wash in amœbic dysentery) have little or no bactericidal action on the dysentery bacillus even in distilled water.

Several of the above antiseptics have been used in the form of a bowel wash in dysentery, and the first three of Table II appear to be

worthy of further careful trial in bacillary dysentery, especially in fairly early severe cases under carefully controlled conditions. In chronic bacillary dysentery the first three organic combinations of silver appear to me very promising for use in the same way. The injection of the first has, indeed, already been followed by apparently very favourable results in a few cases in which I have tried it, and I hope before long to have sufficient experience to enable me to report on their value in a clinical journal.

